thymoma types B2, B3, and, of course, thymic carcinoma. In the case of thymoma (B2, B3), there is good retrospective evidence that local irradiation definitely reduces the rate of recurrences by 20%.

In conclusion, WHO type A, AB, and B1 thymoma types do not need adjuvant treatment, if surgical resection is complete. WHO type B2 and B3, as well as combined tumours and thymic carcinoma profit from adjuvant treatment which should at least be directed to local recurrences (local irradiation) or imply adjuvant chemotherapy (1,10). No prospective clinical studies are available.

Pathogenesis of thymoma-associated autoimmune phenomena

Thymomas are associated to a large variety of autoimmune phenomena where myasthenia gravis is the most frequent and classical paraneoplastic autoimmune disease. A detailed functional analysis of thymoma associated with myasthenia gravis reveals that these tumours produce and export autoreactive CD4+ T cells into the periphery (while thymomas not associated to myasthenia gravis do not). A major effect related to the generation of autoimmune disease may be attributed to the finding that within these tumours the production of adequate numbers of regulatory T cells (CD4+, CD25+) is significantly decreased (10,11). Further pathogenetic findings related to thymomas associated myasthenia gravis shows that polymorphisms in the co-stimulatory receptor CTLR4 with high expression is found in patients with thymoma (2). Furthermore, the already cited hemizygous expression of MHC molecules is definitely a factors increasing the overall probability of autoimmune diseases in these patients. The findings imply that tumour-associated intratumourous defects of T cell differentiation are the reason for these autoimmune diseases and that different pathogenetic pathways may play a role.

Differential diagnosis of thymic carcinoma

Mediastinal involvement by carcinoma may be derived from different primary sites. The differential diagnosis of squamous cell carcinoma of thymus vs. lung is the most challenging problem. Some topographic and structural features favour a thymic origin:

If the squamous cell carcinoma is adjacent to thymoma or combined with thymoma type B3, a thymic origin is very likely. Prominent perivascular spaces in the tumour and the overall lobular architecture also suggests thymic squamous cell carcinoma (TSCC). Furthermore, immunohistochemical findings may help: thymic squamous cell carcinomas often express CD5 and CD70, and may contain myoid cells (similar to the normal thymus). The value and sensitivity of CD5 expression in the most frequent subtype (SCC) is about 60%, but the specificity in squamous cell carcinoma is almost absolute. Another highly sensitive and specific marker is the expression of the c-kit tyrosin kinase receptor (CD117). Expression is found In squamous cell carcinoma of the thymus in 90% whereas it is seen in pulmonary squamous cell carcinoma only in 5% (8). Further differences reside on genetic characterization. A typical loss of the long arm of chromosome 16 (16q-) or the combination of 16q- with deletions on chromosome 6 or amplification of chromosome 18 are highly predictive for a primary thymic tumour in comparison to lung or squamous cell carcinoma of the upper respiratory track.

Conclusion

The diagnosis of thymoma and thymic carcinoma is now in a stage where an agreed histopathological classification is accepted. The rules of this classification have to be learnt but are highly reproducible in all published series. This classification will help to elaborate therapeutic protocols for prospective clinical studies. The variability of clinical presentation and behaviour still requires several clinicopathologic correlations. Modern techniques of immunostochemistry, molecular techniques and gene expression will improve the diagnosis and open new horizons for an indiviualized therapy.

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E13-02 Insights into Thymic Epithelial Tumor, Tue, Sept 4, 16:00 – 17:30

Insights into Thymic Epithelial Tumor: Imaging Findings

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Thymic epithelial tumors (TET) are uncommon, with a broad spectrum of biologic and morphologic features. Of several proposed classifications, WHO histologic classification reflects both the clinical and the functional features of TET and thus contributes to the clinical assessment and treatment of patients with these tumors (1, 2). Recently, several reports described specific CT, MR imaging, and FDG-PET features of TET that reflect the WHO histologic subtypes (3-7). In this section, we discuss imaging features of TET correlated with histologic subtypes.

Computed Tomography (CT)

Because of embryologic background and anatomic location, TET can occur adjacent to the junction of the great vessels and the pericardium; less commonly, in the cardiophrenic angles or adjacent cardiac borders; and, rarely in the neck or other mediastinal compartments (8). CT has a much higher sensitivity for detecting TET than conventional radiography, and also allows evaluation of (a) invasion of the surrounding mediastinal fat, vascular structures, and adjacent lung; and (b) the presence of pleural and extrapleural seeding. On CT scans, TET usually appear as homogeneous, oval, rounded or lobulated soft-tissue masses in the anterior mediastinum (8). In cases of invasive thymoma or thymic carcinoma, invasion of the mediastinal fat or adjacent structures as well as pleural seeding may be seen.

Tomiyama et al (3) assessed the CT features of various subtypes of TET and reported that smooth contours and a round shape are most suggestive of type A tumors, irregular contours are most suggestive of type C tumors, and calcification is suggestive of type B tumors. Jeong et al (5) reviewed the CT findings correlated with simplified WHO classification of TET (low-risk thymomas (type A, AB, and B1); high-risk thymomas (type B2 and B3); thymic carcinomas (type C)) and prognosis. CT findings that are more common in high-risk thymomas and thymic carcinomas include lobulated contour, mediastinal fat invasion, and great vessel invasion. Findings associated with significantly more frequent recurrence and metastasis include lobulated or irregular contour, oval shape, mediastinal fat invasion or great vessel invasion, and pleural seeding.

MR Imaging

At MR imaging, types A, AB, and B1 thymomas have similar or slightly higher signal intensity (SI) than that of muscle on T1-weighted images (T1WI) and higher SI than that of muscle on T2-weighted images (T2WI) (4, 6, 9-12). At Gd-DTPA enhanced MR imaging, homogeneous and moderate enhancement is observed. Most B2 and B3 thymomas manifest inhomogeneous SI with scattered high-intensity areas on T2WI, which are corresponded to cystic spaces with or without hemorrhage on pathologic examination (6). In a study by Sakai et al (6), T2WI indicated that six of 12 invasive thymomas (probably WHO type B2 or B3) had lobular internal architecture, with 1- to 2-mm-thick low SI lines; for the five benign thymomas (probably WHO type A, AB, B1), this was not, however, the case. Unlike types A, AB, B1, B2, and B3 tumors, thymic carcinomas show relatively low SI at both T1- and T2WI, appearing as slightly inhomogeneous lesions (12).

FDG- PET

In TET, FDG-PET may be useful in differentiating thymic carcinoma from other thymic tumors, thymic hyperplasia, and normal physiologic uptake (13). Sasaki et al (7) reported that the standardized uptake value (SUV) for thymic carcinoma was significantly greater than that for invasive or non-invasive thymoma. With an SUV cutoff point of 5.0, thymic carcinoma can be differentiated from thymoma with reasonably high sensitivity (84.6%), specificity (92.3%), and accuracy (88.5%). There was no statistically significant difference in SUV between invasive and non-invasive thymomas.

Conclusions

An awareness of the various imaging findings of the different types of TET, as reflected in the WHO histologic classification, may be helpful in clinical practice for the assessment and treatment of patients with TET.

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E13-03 **Insights into Thymic Epithelial Tumor, Tue, Sept 4, 16:00 – 17:30**

Outcome of surgical treatment for thymic epithelial tumors

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Background: Thymoma, thymic carcinoma, and thymic carcinoid are derived from the epithelium of the thymus, and are described as Thymic epithelial tumors. These neoplasms are well-known for heterogeneity in the oncological behaviors, variability in the histological appearance, and association with autoimmune diseases represented by myasthenia gravis. The main strategy of treatment for thymic epithelial tumors is supposed to be surgical resection. There have been many reports studying prognostic factors including Masaoka staging system, completeness of resection, size of the tumor, the involved organs, and association with myasthenia gravis. On the other hand, pathological classification of thymic epithelial tumors has been confusing and the clinical significance of histological appearance has been unclear. World Health Organization (WHO), however, established a consensus on the histological classification of the thymic epithelial tumors in 1999.

Aim: We aimed to elucidate the prognostic factors responsible for survival, and examined the outcome of surgical treatment based on 272 patients between 1957 and 2001.

Results: The number of patients according to Masaoka stage is 113 in stage I, 64 in stage II, 71 in stage III, 11 in stage IVa, and 13 in stage IVb. The number of patients according to World Health Classification system is 17 in type A, 65 in type AB, 50 in type B1, 89 in type B2, 23 in type B3 and 28 in type C.

The proportion of invasive tumor was 11%, 42%, 47%, 69%, 85%, and 94%, in type A, AB, B1, B2, B3, and C tumor, respectively. The proportion of tumors with involvement of the great vessels was 0%, 4%, 7%, 17%, 19% and 43% in type A, AB, B1, B2, B3, and C tumor, respectively. The proportion of association with myasthenia gravis was 0%, 7%, 40%, 56%, 10%, and 0% in type A, AB, B1, B2, B3, and C tumor, respectively.

According to Masaoka staging system, 10-year survival rate was 99%, 95%, 91%, 36% and 0% in stage I, II, III, IVa and IVb disease, respectively. According to WHO histological classification system, 10-year survival rate was 100%, 96%, 97%, 92%, 78% and 68% in type A, AB, B1, B2, B3, and C tumor, respectively.

Multivariate analysis was done to determine the independent prognostic factor in thymomas. Masaoka staging system and WHO histologic classification were the significant factors while age, gender, association with myasthenia gravis, completeness of resection or involvement of the great vessels were not.

Conclusion: Stage and histology are significant prognostic factors and should be considered when determining the strategy for treatment.

E13-04 **Insights into Thymic Epithelial Tumor, Tue, Sept 4, 16:00 – 17:30**

Radiation therapy for thymic epithelial neoplasms

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Pre-operative Radiation Therapy

For locally advanced, large, invasive thymomas that are unresectable or marginally resectable, preoperative adjuvant radiation therapy has been advocated to render it resectable. Several studies on limited numbers of

